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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
08/908,867	08/08/97	YOUNG	A 227/166

EXAMINER	
HOLLERAN, A	
ART UNIT	PAPER NUMBER
1642	21

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HM22/0227

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary

Application No.	Applicant(s)
08/908,867	Young et al.
Examiner	**Group Art Unit**
Anne Holleran	1642

☒ Responsive to communication(s) filed on *Jan. 14. 2000*

☐ This action is **FINAL.**

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire *3* month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claim

☒ Claim(s) *1-11 and 20-30* is/are pending in the applicat

Of the above, claim(s) _____ is/are withdrawn from consideration

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) *1-11 and 20-30* is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐ approved ☐ disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☒ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____.

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☐ Notice of References Cited, PTO-892

☐ Information Disclosure Statement(s), PTO-1449, Paper No(s). _____

☐ Interview Summary, PTO-413

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

DETAILED ACTION

1. This Office Action is responsive to the Amendment filed January 14, 2000.

Claims 12-19 were canceled.

Claims 22-30 were added.

Claims 1-11 and 22-30 are pending and examined on the merits.

2. The response to the Notice to Comply regarding sequence rules, filed May 9, 2000, is acknowledged. This application now complies with the requirements of 37 C.F.R. §§ 1.821-1.825.

Applicant's attention is drawn to a correction made in the Sequence Listing CRF for SEQ ID NO: 35. The Office corrected the alignment of the amino acid numbering. Please see the attached copy of the Raw Sequence Listing report for SEQ ID NO: 35.

3. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

Claim Rejections Withdrawn:

4. The rejection of claims 4 and 5 under 35 U.S.C. 103(a) as being unpatentable over Dupre et al (supra) in view of Rai et al (supra) is withdrawn upon further consideration.

5. The rejections of claims 9-11 under 35 U.S.C. 103(a) as being unpatentable over Dupre et al (supra) in view of Daniel et al (Daniel, O. et al. British Medical Journal, 3: 720-722, 1974) and further in view of Eng (supra) is withdrawn upon further consideration.

Claim Rejections Maintained and New Grounds of Rejection:

6. The rejection of claims 1-11, 20 and 21 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention is maintained and further applied to new claims 22-30. New grounds of rejection are presented.

The rejection of Claim 1 as vague and indefinite on the grounds that "therapeutically effective amount" is unclear is maintained. Because claim 1 is drawn to a method for beneficially regulating gastrointestinal motility and because "beneficial" regulation of gastrointestinal motility is not an experimental endpoint, it is not clear what therapeutic effect is to be brought about. Thus, without a clear and measurable endpoint, the phrase "therapeutically effective amount" has no meaning and does not provide a limitation to the method step of administering an exendin or an exendin agonist.

Claim 1 is vague and indefinite because it is not clear what is encompassed by the term "exendin". The specification describes exendins as polypeptides found in the venom of the Gila monster and the specification provides examples of exendin-3, exendin-4 and exendin (9-39).

However, the specification does not provide guidance as to what compounds are included in the term "exendin". Is it any peptide found in the venom of the Gila monster ?

Claim 1 is vague and indefinite because it is not clear what is encompassed by an "exendin analogue" or an "exendin derivative".

Claims 25-28 are vague and indefinite because they are drawn to methods using exendin derivatives having various percentages of sequence similarity to sequences which are not defined.

7. The rejection of claims 20 and 21 under 35 U.S.C. 112, first paragraph, because the specification does not reasonably provide enablement commensurate with the scope of the claimed invention is maintained. The rejection is also applied to claims 1-11 and new claims 22-30.

Thus, claims 1-11 and 20-30 are rejected under 35 U.S.C. 112, first paragraph, because the specification does not reasonably provide enablement commensurate with the scope of the claimed invention. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

Factors to be considered in determining whether undue experimentation would be required to practice the full scope of the claimed invention are: 1) quantity of experimentation necessary; 2) the amount of direction or guidance presented in the specification; 3) the presence or absence of working examples; 4) the nature of the invention; 5) the state of the prior art; 6) the relative

skill of those in the art; 7) the predictability or unpredictability of the art; and 8) the breadth of the claims. See Ex parte Forman, 230 USPQ 546, BPAI, 1986.

The claimed methods are broad in scope because the claimed inventions are drawn to methods of treatment of a broad range of conditions. Claims 1, 4-11 and 20-30 drawn to methods for beneficially regulating gastrointestinal motility. Although the specification provides some examples of "beneficial" regulation of gastrointestinal motility, such as reducing gastric motility, delaying gastric emptying or gastrointestinal spasm, the specification does not provide guidance as to what other physiological events are encompassed by the term "gastrointestinal motility". The specification confines its examples to demonstrating the effect of exendin-3 and exendin-4 on gastric emptying. It is not clear from the specification or from any teachings in the prior art that gastric emptying is a physiological process that is regulated by the same mechanisms as gastric motility, gastrointestinal spasm or any physiological process that may be encompassed by the term "gastrointestinal motility".

The claimed methods are also broad in scope because the claimed inventions are drawn to methods comprising the use of exendin analogs or exendin derivatives. The specification does not provide a clear definition of what compounds are encompassed by the term "exendin". Without a definition of the metes and bounds of what is an exendin and what is not, the specification cannot possibly provide guidance as to what compounds are encompassed by the terms "exendin analog" or "exendin derivative". Furthermore, the terms "analog" and "derivative" are defined with open language and appear to encompass compounds which have structural similarity with or which are

functionally defined as having a similar effect as an exendin on gastrointestinal motility. Thus, the terms "exendin analog" and "exendin derivative" encompass a group of compounds which vary widely in structure because "exendin" itself is not defined structurally and because it is not clear which parts of an exendin peptide are to be retained in an "analog" or "derivative". Moreover, there does not appear to be support in the specification for a functional limitation because the specification does not provide adequate guidance to enable one of skill in the art to understand how exendin-3 or exendin-4 function to regulate all physiological functions encompassed by "gastrointestinal motility".

The guidance provided in the specification is not adequate to support the full scope of the claimed inventions. The specification merely teaches that exendins are found in the venom of the Gila monster but not supply any evidence that the prior art has defined a genus of peptides referred to as "exendins". The specification also teaches that exendin-3 and exendin-4 inhibit gastric emptying and teach that [9-39]exendin does not block the inhibitory effect of exendin-3 and exendin-4 on gastric emptying thus indicating that exendin-3 and exendin-4 do not mediate their effects on gastric emptying by binding to the GLP-1 receptor and the results of the experiments indicate that exendin-3 and exendin-4 may bind to an "exendin" receptor to mediate their effects on gastric emptying. However, this teaching does not establish the identity of the an "exendin" receptor. The prior art does teach an "exendin" receptor but the specification does not establish that the prior art "exendin" receptor is the same as the "exendin" receptor which mediates the inhibition of gastric emptying by exendin-3 and exendin-4. Furthermore, the

specification does not establish that this receptor is present over the entire gastrointestinal tract and would mediate any type of gastrointestinal motility.

New claims 22-30, dependent from claim 1, recite limitations which limit the range of activity of the exendin analog or derivative to a percentage of the activity of any exendin (claims 22-24), which limit the sequence similarity to any exendin of the exendin analog or derivative (claims 25-28), limit the analogs or derivatives to analogs or derivatives of exendin-4 (claim 29) and limit the subject to a human subject (claim 30). The limitations provided by claims 22-28 do not limit the scope of the claimed methods to what is enabled by the specification because the activity of all exendins is not described and because the amino acid sequence of all exendins have not been described. The limitation provided by claim 29 does not limit the scope of the claimed method to what is enabled because the specification does not adequately describe what is meant by the term analog or derivative. The limitation provided by claim 30 does not limit the scope of the claimed method to what is enabled because confining the methods to use in humans does not remedy any of the deficiencies of the specification.

Applicant has argued that patent applicants are not required to disclose and test every species that may be encompassed by their claims and cites, among other cases, *In re Fuetterer*, 138 USPQ 217 (CCPA 1963), to support the position that the breadth of a claim is not a sufficient basis for making an enablement rejection. However, Applicant's arguments are not found persuasive. In the case of *In re Fuetterer* the issue to be decided was whether an element of a claimed combination (a rubber stock for producing tire treads), an inorganic salt, was clearly

and unambiguously claimed so that the claimed combination was clearly and unambiguously claimed; and whether the functional language used to describe the inorganic salt placed and undue burden on the public. The court found that no undue burden was placed on the public by a claim to a rubber stock which comprised, among other ingredients, any inorganic salt with the ability to "hold[ing] a mixture of said carbohydrate and protein in colloidal suspension in water" because the claimed invention was directed to a combination for which the inorganic salt was but one element and because the functional language used to define the inorganic salt was particularly pointed out and distinctly claimed in compliance with second paragraph of section 112.

In the instant case, the issue to be decided is whether the specification enables the full scope of the use of exendins, exendin analogs, exendin derivatives, and any of the compounds of either of claims 20 or 21 for the beneficial regulation of gastrointestinal motility. In the instant case, the claimed inventions are drawn to methods comprising the administration of a genus of compounds which are not particularly pointed out and distinctly claimed. Thus, following the guidance of *In re Fuetterer*, it would be an undue burden for one of skill in the art to practice the invention as claimed because the specification provides no guidance as to what compounds are included within the term "exendin".

With regard to claims 20 and 21, where the genus of compounds is described by a chemical formula of a peptide sequence, because the specification lacks a description of the physiological basis for how the exemplified exendins exert their effects to inhibit gastric emptying, the limited examples cannot be extrapolated to all other "exendins", or derivatives or analogs

thereof or to any of the compounds encompassed by the chemical formula which expressly excludes the exemplified embodiments. Furthermore, because the specification lacks a description of how the effects on gastric emptying may be extrapolated to any type of gastrointestinal motility, the limited examples demonstrating inhibition of gastric emptying may not be used by one of skill in the art to enable the full scope of claims to methods of regulating gastrointestinal motility.

8. The rejection of claims 1-3 under 35 U.S.C. 102(b) as being anticipated by Dupre et al (Dupre, J. et al. Diabetes, 44: 626-630, 1995) as evidenced by either Goke et al (Goke, R. et al. J. Biol. Chem., 268(26): 19650-19655, 1993) or Rai et al. (Rai, A. et al. Am. J. Physiol., 265: G118-G125, 1993) is maintained.

Applicant's arguments that GLP-1[7-36]amide cannot be considered an exendin analog or exendin derivative have been considered but not found persuasive. The specification does not adequately describe the metes and bounds of exendin, exendin derivatives and exendin analogs. For example, an exendin derivative may be a compound which comprises only 1 amino acid "derived" from an exendin. Applicant's arguments also point to limitations that do not appear in the claims, such as differences in potency and differences in receptor binding. Thus, the rejection is maintained for the reasons of record.

9. The rejection of claims 6-8 under 35 U.S.C. 103(a) as being unpatentable over Dupre et al (supra) in view of either Chernish et al (U.S. Patent 3,862,301, Chernish, S.M. et al., published January 21, 1975) or Kolterman et al (WO 95/07098, Kolterman, O. et al., published March 16, 1995) and further in view of Eng (U.S. Patent 5,424,286, Eng, J., published June 13, 1995) is maintained and further applied to claims 1-3.

Applicant's arguments have been considered but not found persuasive. Applicant's arguments turn on whether or not Dupre teaches a method of inhibiting gastric emptying comprising administering an exendin analog or exendin derivative and supports the argument by stating that GLP-I(7-36)amide is not an exendin analog or exendin derivative. As discussed above, this argument is not found persuasive and the rejection is maintained for the reasons of record.

10. Claim 25 is rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The basis for this rejection is that new claim 25 introduces new matter into the specification.

Claim 25 is drawn to a method of claim 1 wherein the exendin derivative has at least about 50% sequence similarity to he exendin of which it is an analog or derivative. The passage pointed

to by Applicant as containing support for the new claims does not provide specific support for an embodiment of the claimed methods wherein the exendin derivative used in the invention methods has at least 50% sequence similarity. Thus, claim 25 introduces new matter into the specification and is not supported by the specification as filed. Thus, one of skill in the art would not find that Applicant was in possession of the claimed invention at the time the invention was filed.

Conclusion

No claim is allowed. This rejection contains new grounds of rejection is not made final. Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Anne Holleran, Ph.D. whose telephone number is (703) 308-8892. Examiner Holleran can normally be reached Monday through Friday, 9:00 am to 5:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Anthony Caputa, Ph.D. can be reached at (703) 308-3995.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist at telephone number (703) 308-0196.

ALH

Anne L. Holleran
Patent Examiner
February 23, 2001

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